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Predictive factors of acute kidney injury in patients undergoing rectal surgery

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Abstract

Background: Despite major advance in surgical techniques from open surgery to robot-assisted surgery, acute kidney injury (AKI) is still major postoperative complication in rectal surgery. The purpose of this study is to compare the incidence of postoperative AKI according to different surgical techniques and also the risk factors, outcomes of AKI in patients undergoing rectal cancer surgery.
Methods: A retrospective medical chart review was done in a total of 288 patients who received proctectomy because of rectal cancer from 2011 to 2013.
Results: The mean patient age was 62 ± 12 years, and male was 64.2%. Preoperative creatinine was 0.91 ± 0.18 mg/dL. Open surgery was performed in 9%, and laparoscopy assisted surgery or robot assisted surgery were performed in 54.8% or 36.1% of patients, respectively. AKI developed in 11 patients (3.82%), 2 (18%) of them received acute hemodialysis. Incidence of AKI was not different according to the surgical technique, however, the presence of diabetes, intraoperative shock, and postoperative ileus was associated with the development of AKI. In addition, AKI patients showed significantly longer hospital stay and higher mortality than non-AKI patients.
Conclusion: Our study demonstrated that despite advances in surgical techniques, incidence of postoperative AKI remains unchanged and also that postoperative AKI is associated with poor outcome. We also found that presence of diabetes, intra-operative shock and postoperative ileus are strongly associated with the development of AKI. More careful attention should be paid on high risk patients for the development of postoperative AKI regardless of surgical techniques.

Introduction

Acute kidney injury (AKI) is commonly seen in the post-operative period and is consistently associated with increased rates of mortality and morbidity [1,2]. Postoperative AKI frequently occurs after cardiac surgery (frequency, 48–94%) or liver transplantation (frequency, 25%), thus clinical characteristics, risk factors, or outcomes of AKI in these clinical situations have been extensively studied. However, only a few studies addressed AKI after colorectal surgery, which has different pathophysiology with cardiac surgeries or transplantation.

In regard to colorectal surgery, laparoscopic surgery is now considered as the approach of choice for the surgical treatment

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of colon and rectal diseases. In contrast, robotic-assisted laparoscopic surgery is gaining more acceptance recently and showed comparable short-term outcomes as compared with conventional laparoscopic surgery. Although the routine use of the robotic platform for colorectal surgery is not supported because of longer operative time and higher expenses than laparoscopic surgery, robotic surgery is the main indication in cases of rectal or pelvic surgeries.

To our knowledge, it is the first study that assessed the incidence of postoperative AKI in patients who underwent robotic assisted rectal surgery compared with conventional laparoscopic surgery. We compared the clinical characteristics between the AKI and the non AKI groups, and identified perioperative factors that predispose patients to AKI in this population as well as prognosis.

Methods

Ethics statement

The Institutional Review Board of Korea University Anam Hospital approved this study (ED10066-001).

Patients and study design

Patients aged 18 years or older who underwent elective rectal resection admitted to the division of the colo-rectal surgery of the Korea University Anam Hospital (Seoul, Korea) between July 2011 and January 2013 were included.

Exclusion criteria were baseline estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2, end stage renal disease on maintenance renal replacement therapy (RRT) or AKI developed in the week before surgery. Preoperative baseline serum creatinine (SCr) values were defined as the most recent SCr (mg/dL) measured within 30 days of the surgery.

The primary outcome was the development of postoperative AKI within 7 days after surgery, and postoperative AKI was diagnosed according to the Acute Kidney Injury Network criteria (i.e., $\geq$ 0.3 mg/dL or a $\geq$ 50% increase in the SCr level from the baseline value within 48 hours or a urine output < 0.5 mL/kg/h for $\geq$ 6 hours). The eGFR was calculated using the Modification of Diet in Renal Disease equation.

Patient electronic hospital database were reviewed to collect the following variables: patients' demographics (age and sex), preoperative patient characteristics (comorbidity, namely, diabetes mellitus, hypertension, CKD, heart failure and stage of malignancy; albumin, total cholesterol, and SCr), surgical procedure (open, laparoscopy, robotic), intraoperative patient characteristics (operation time, intraoperative shock, and bleeding), and postoperative data need for RRT, total hospital stay, and in-hospital mortality.

An ejection fraction of less than 50% in echocardiography was the criteria for diagnosing heart failure. Postoperative ileus was diagnosed if both passage of flatus or stool and tolerance of oral diet did not occur before day 4 combined with gaseous dilatation of intestine more than 3 cm in simple postoperative abdominal x-rays taken postoperatively [3]. The diagnosis of postoperative infection was made when fever higher than 38°C on more than one occasion and elevated serum C-reactive protein within one week were present.

Statistical analysis

SPSS software, version 19.0 (SPSS Inc., Chicago, IL, USA), was used for statistical analyses. Comparisons between the 2 groups were performed using the Student *t* test or the Mann–Whitney *U* test for numerical data and the chi-square test or Fisher exact test for categorical data.

To identify the risk factors for the development of AKI, we initially conducted univariate analysis, and variables that were statistically significant (P < 0.05) in the univariate analyses were then included in the multivariate analysis with forward conditional elimination of data. Data are presented as odds ratios (ORs) with 95% confidence intervals. A 2-tailed P value < 0.05 was considered significant.

Table 1. Preoperative characteristics, type of surgery, and intraoperative characteristics

Characteristics	All (N = 288)	Non-AKI (N = 277)	AKI (N = 11)	P
Age (y)	62 ± 12	62 ± 12	59 ± 17	0.535
Sex (male)	185 (64.2)	176 (63.5)	9 (81.8)	0.215
Baseline Cr (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	1.0 ± 0.2	0.044
Hypertension	101 (35.1)	95 (34.3)	6 (54.5)	0.060
Diabetes mellitus	44 (15.3)	41 (14.9)	3 (27.3)	0.020
Heart failure (EF < 50%)	11 (3.8)	10 (3.6)	1 (9.1)	0.765
Albumin (g/dL)	4.0 ± 0.4	4.1 ± 0.4	3.9 ± 0.7	0.351
Total cholesterol (mg/dL)	172.3 ± 39.9	172.0 ± 40.0	181.5 ± 39.9	0.568
Operation time (min)	275 ± 99	274 ± 100	293 ± 59	0.132
Intraoperative bleeding (mL)	198 ± 318	193 ± 311	323 ± 471	0.179
Intraoperative shock	49 (17.0)	45 (16.2)	4 (36.4)	0.050
Laparoscopy-assisted surgery	156 (54.2)	150 (54.2)	6 (54.5)	0.979
Robot-assisted surgery	107 (37.2)	102 (36.8)	5 (45.5)	0.561
Concurrent CRTx	22 (7.3)	21 (7.7)	1 (6.3)	1.000
Preoperative CTx	2 (0.9)	2 (0.9)	0	1.000
Adjuvant CTx	110 (38.2)	108 (39.1)	2 (18.2)	0.244
Postoperative infection	13 (4.5)	10 (3.6)	3 (27.3)	0.010
Postoperative bowel ileus	75 (27.4)	67 (25.5)	8 (72.2)	0.002

Data are presented as n (%) or mean ± SD.
AKI, acute kidney injury; Cr, creatinine; CRTx, chemoradiotherapy; CTx, chemotherapy; EF, ejection fraction.

Results

Study population

During the study period, a total of 288 patients met the inclusion criteria. Mean patient age was 62 ± 12 years, and 64.2% of the patients were male (Table 1). The most common comorbidities were hypertension in 35.1%, diabetes mellitus in 15.3%, and heart failure in 3.8%. The stage of colorectal cancer I, II, or III were found in 63%, 6%, and 31% respectively, and preoperative or adjuvant chemotherapy was performed in 0.7% and 37.5% of cases.

For surgical techniques, open laparotomy was performed in 8.7% and laparoscopic- and robot assisted surgeries were performed in 55.1% and 36.2% of patients, respectively. Laparoscopic or robot-assisted resections of rectal cancer were performed by a single surgeon. This surgeon had previously performed more than 600 laparoscopic proctectomies.

The mean SCr level was 0.9 ± 0.2 mg/dL, and 11 patients (3.8%) developed AKI within 7 days after surgery; 6 patients (55%) were at stage 1, 1 patient (9%) was at stage 2, and 4 patients were at stage 3 (36%). The rates of postoperative AKI did not show any difference between patients with different surgical techniques; open laparotomy, laparoscopic-assisted surgery, and robot-assisted surgery: 3.8%, 6%, and 4.6%.

Comparison between patients with or without AKI

The characteristics of patients with and without AKI are summarized in Table 1. Comparing with non-AKI group, patients with postoperative AKI were more likely to have preexisting hypertension [95 (34.3%) vs. 6 (54.5%), $P = 0.06$] and diabetes mellitus [41 (14.7%) vs. 3 (27.3%), $P = 0.02$]. Additionally, patients were more likely to have higher preoperative SCr (0.9 ± 0.2 vs. 1.0 ± 0.2 mg/dL, $P = 0.044$).

Intraoperative shock, postoperative infection, and bowel ileus were more frequently associated with postoperative AKI than non AKI group [shock 45 (16.2%) vs. 4 (36.4%), $P = 0.05$; infection 10 (3.6%) vs. 3 (27.3%), $P = 0.01$; bowel ileus 67 (25.5%) vs. 8 (72.2%), $P = 0.002$]. Although patients who underwent robotic surgery had lower rate of hypertension and diabetes mellitus and similar level of SCr than those who underwent laparoscopic surgery, development of intraoperative shock and postoperative ileus was greater or comparable in patients with robotic surgery (Table 2).

Robotic surgery, expected to have better results, did not show difference in the development of postoperative AKI compared with open surgery or laparoscopic surgery.

Table 2. Characteristics of patients undergoing laparoscopic surgery or robotic surgery

Characteristics	Laparoscopic surgery ($N = 156$)	Robotic surgery ($N = 107$)	P
Baseline Cr (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	0.075
Hypertension	63 (40.4)	29 (27.1)	0.035
Diabetes mellitus	34 (21.8)	8 (7.5)	0.002
Intraoperative shock	21 (13.5)	25 (23.4)	0.047
Postoperative bowel ileus	40 (25.5)	27 (26.2)	1.000

Data are presented as n (%) or mean ± SD.
Cr, creatinine.

Table 3. Independent risk factors of postoperative acute kidney injury in patients undergoing rectal cancer surgery

Risk factors	Multivariate analysis		
	Odds ratio	95% CI	P
Diabetes mellitus	3.487	0.843–14.422	0.040
Intraoperative shock	3.799	0.941–15.343	0.060
Postoperative bowel ileus	6.751	1.504–28.779	0.010

CI, confidence interval.

Risk factors of development of AKI

To evaluate the independent risk factors predicting the development of postoperative AKI, multivariate analysis using a logistic regression model was performed (Table 3). Preoperative variables that were significant in univariate analysis, such as blood urea nitrogen, creatinine, hypertension, diabetes mellitus, intraoperative shock, postoperative infection, and postoperative ileus, were included in multivariate analysis. However, odds ratio of robot assisted surgery to develop AKI was not statistically significant (OR: 1.4306, $P = 0.563$). In multivariate analysis, diabetes mellitus, intraoperative shock and postoperative ileus were found to be the independent risk factors of AKI after rectal cancer surgery. Notably, among the risk factors of postoperative AKI, postoperative ileus more strongly increased the risk of AKI after rectal surgery (OR: 6.751, $P = 0.01$; Table 4).

Clinical outcomes of AKI patients

Two of the 11 patients with AKI (18%) received RRT (1 patient was treated with continuous venovenous hemodiafiltration and 2 patients with intermittent hemodialysis). Patients with postoperative AKI had prolonged hospital stay (16 ± 10 vs. 26 ± 16 days, $P = 0.044$) and had higher in-hospital mortality than those patients who did not develop AKI (13% vs. 0%, $P < 0.001$).

At 6 months after surgery, mean of SCr remained higher in patients with AKI than those without AKI (1.2 ± 0.4 vs. 0.9 ± 0.2 mg/dL, $P = 0.029$). Although SCr at 6 month was higher in AKI group, changes in eGFR 6 month after rectal surgery was comparable between the two groups.

Discussion

AKI is a frequently occurring complication after major surgery which increases morbidity and mortality [4]. Especially,

Table 4. Comparison of outcomes between non-AKI and AKI patients

Characteristics	All ($N = 288$)	Non-AKI ($N = 277$)	AKI ($N = 11$)	P
Total hospital stay (d)	17 ± 10	16 ± 10	26 ± 18	0.044
POD 6 mo creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.2	1.2 ± 0.4	0.029
ΔeGFR (mL/min/1.73 m^2)	0.9 ± 14.8	1.1 ± 14.5	−0.8 ± 21.7	0.416
Need for dialysis	2 (0.7)	0	2 (18.2)	0. 001
In-hospital mortality	2 (0.7)	0	2 (18.2)	0.001

Data are presented as n (%) or mean ± SD.
AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; POD, postoperative day.

AKI after cardiac or vascular surgery is well known because of its high prevalence, ranging from 20% to 30%, with drastic outcomes [5,6]. In contrast to cardiac or vascular surgery, the incidence or risk factors after intraperitoneal surgery have not been studied widely due to paucity of data. Our group previously reported the incidence of postoperative AKI after liver surgery was 7.6% with poorer outcome in these patients [7]. In this study, we retrospectively analyzed the incidence, predictors, and impact on outcome of AKI in 288 patients who underwent rectal surgery. Overall rate of AKI after rectal surgery was 3.8%, and this frequency was lower than previous reported incidence of postoperative AKI in patients with colorectal surgery (11.8%) [8]. Lower incidence of postoperative AKI in our study is likely to be associated with narrow inclusion criteria that included only patients with rectal cancer and excluding patients with colon cancer.

Interestingly, we also found that there was no difference in the incidence of AKI according to the operation method (3.8% vs. 4.6% vs. 6%; open surgery vs. laparoscopy-assisted surgery vs. robot-assisted surgery). Currently, laparoscopic colorectal surgery is well established and has shown satisfactory oncologic and surgical outcomes in many prospective randomized trials compared with open laparotomy [9]. Although laparoscopic surgery has been widely accepted for colonic resection, its application in rectal cancer continues to be challenging [10] because rectal cancer surgery is performed with limited surgical instruments within confined space and demands more technical expertise than colectomy. Robotic approach has been developed to overcome these limitations of laparoscopic surgery in rectal cancer, providing 3-dimensional, high-definition views and multiarticulated instruments to a surgeon with ergonomically ideal procedure. Although many studies have shown that robotic approach can be performed safely in rectal cancer surgery, whether robotic rectal surgery enable improved postoperative outcomes in comparison with laparoscopic surgery is not fully elucidated. In this study, with regard to postoperative AKI, laparoscopic or robotic assisted rectal surgery showed the comparable results. Although patients with rectal cancer were not randomly assigned to laparoscopic or robot assisted surgery, there was no significant differences in baseline SCr between patients with either surgical techniques.

Intraoperative factors including operation time which in other studies have shown to be important predictive factors of postoperative AKI was comparable as well. Similar to our study, 2 comparative studies addressed that the operating time of robotic surgery was not shorter than laparoscopic surgery; Kwak et al [11] reported mean operative time of 270 minutes for robotic group and 228 minutes for laparoscopic group, and Baek et al [12] reported that a mean of 296 minutes for robotic procedures and 315 minutes for laparoscopic procedures ($P = 0.357$). Unlike our expectations that robotic surgery would shorten operation time through advanced instruments and as a result decrease the rate of postoperative AKI, there was no difference in operation time nor incidence of AKI between the 2 different surgical techniques.

To determine the major risk factors of postoperative AKI, we next performed multivariate regression analysis and found out that postoperative paralytic ileus was the potent independent predictors of AKI after rectal surgery. Although direct linkage between postoperative ileus and development of AKI is not clear, the predominant mode of kidney injury is assumed to be due to intra-abdominal hypertension (IAH). Two studies [13,14] reported development of ileus to be a risk factor for IAH among mixed intensive care unit patients, and animal data and human observational studies indicate that AKI are early and frequent consequence of IAH [15].

Regarding connection of postoperative ileus with AKI, enhanced intestinal bacterial translocation during ileus might also be another feasible mechanism leading to development of AKI. Intestinal bacteria easily transmigrate during ileus [16], and limited but recent data indicating that intestinal microbiota affects the outcome of AKI support this hypothesis [17]. Recently, intestinal microbiota and kidney cross talk in AKI have the limelight for explaining the inflammatory pathogenesis of AKI, however, the exact mechanisms are unknown.

It is well known that preoperative comorbidities, including diabetes, hypertension, and CKD, are strong risk factors of postoperative AKI [8,18]. We also identified that patients with postoperative AKI were more likely to have preexisting diabetes in multivariate analysis. On contrary, baseline creatinine had no impact on development of postoperative AKI in our study due to excluding the patients with CKD. Hypertension and robotic surgery were not a risk factor in our study as well.

Despite several interesting findings, there are several limitations in this study. Because data were retrieved from single center, possible systemic problems intrinsic to our center may not be applicable to other centers. The other is the inherent limitations with retrospective design with a relatively small number of patients who were not randomly assigned according to a surgical techniques. Additionally, we were not able to conclude about the exact mechanisms contributing to development of AKI in patients with paralytic ileus after rectal surgery. In order to prove increased intra-abdominal pressure after rectal surgery mediated the postoperative AKI, measuring intra-abdominal pressure should have done during postoperative period.

In conclusion, 3.8% of patients with rectal cancer undergoing elective rectal surgery developed postoperative AKI. Although robotic techniques have been mainly used in rectal cancer surgery to overcome inherent limitations of laparoscopic technique, it did not show beneficial effects on incidence of postoperative AKI compared with conventional laparoscopic techniques. We also identified risk factors for AKI after rectal surgery and notably paralytic ileus after surgery was strongly associated with development of postoperative AKI. Presence of postoperative ileus might predict the postoperative AKI, hence in patients with ileus after rectal surgery more careful monitoring is necessary for early detection of AKI.

Conflicts of interest

The authors have no financial conflicts of interest.

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